

Claim 16 has been amended to clarify language describing the nucleotide sequences that encode mature human artemin and mature mouse artemin. Also, the language of the claim has been amended to clarify the functional features of the complementary nucleotide sequence.

Claim 21 has been amended by inserting the ATCC deposit number that was received from the ATCC after the filing date. The number has been added at the location reserved for it on line 15 of page 64.

Claim 23 has been amended by correcting typographical errors in the identification of human and mouse pro-artemin sequence numbers. The correct identification of these sequence numbers is found in the specification at least at page 6, line 24 of the specification.

Claim 25 has been amended by describing the recombinant nucleic acid molecule that encodes artemin as being one that is capable of specifically hybridizing to specific nucleotide sequences. As in claim 15, support for the specified sequences is found in the specification at least at page 7, lines 28 - 32.

Claim 26 has been amended to make the claim an independent claim. Support is found in the original claim.

Claim 27 has been amended to further describe the polynucleotide that encodes a conservatively substituted variant of the artemin sequences of steps (a), (b) or (c) as being capable of specifically hybridizing to a specific nucleic acid sequence. Support for the listed sequences is found in the specification at least at page 8, lines 6 - 13.

Claim 39 has been added. Claim 39 depends from claim 12 and is drawn to a nucleic acid comprising a polynucleotide encoding a pan-growth factor, wherein the characteristics of the non-artemin growth factor of the TGF- β family is further described. Support for the features described in the claim are found in the specification at least at page 32, lines 22 - 31.

Claims 12, 15 - 27 and 39 are in the case.

No new matter has been added.

Objection to the Information Disclosure Statement filed March 5, 1999, as lacking the date of public availability and names of authors for references AF, AG, AI and AJ.

A new Information Disclosure Statement is filed herewith under 37 C.F.R. §1.97(c), along with the fee set forth in 37 C.F.R. §1.17(p). The new IDS describes the four GenBank references that were rejected from the initial IDS. Paper copies of the four references are also enclosed. It is respectfully requested that the new IDS be entered into the case.

Rejection of claims 12, 15, 16, 19 - 23 and 25 - 27 under 35 USC §112, first paragraph, as lacking written description.

It is respectfully requested that the rejection of claims 12, 15, 16, 19 - 23 and 25 - 27 under 35 USC §112, first paragraph, as lacking written description be reconsidered in view of the amendments to the claims and upon consideration of the reasons discussed below and be withdrawn.

The Action states that the specification does not sufficiently describe polynucleotides that encode conservatively substituted variants and naturally occurring allelic variants of artemin polypeptides, and it is argued that mere description of an amino acid sequence, including conservatively substituted variants, is not a suitable description of the encoding nucleic acid -- a description of the nucleic acid itself is required.

Claims 12, 15, 25 and 27 (the independent claims that describe polynucleotides that encode variants of artemin polypeptides) have been amended so that they now further describe such polynucleotides as containing from at least 15 to about 10,000 nucleotides, and being capable of specifically hybridizing to at least one of a group of artemin nucleotide sequences. The nucleotide sequences that encode for artemin that are now described in the amended claims are for human and mouse artemin sequences (SEQ ID NOS:6 - 8, and 37 - 39, respectively), and to the respective complementary sequences (SEQ ID NOS:9 - 11, and 60 - 62). The reference in claims 15 and 25 to a "nucleic acid complementary thereto" has been deleted in favor of the direct recitation of the complementary artemin sequences to which the claimed sequences will hybridize. Therefore, the claimed polynucleotides are now described as being capable of encoding an artemin polypeptide or a conservatively (amino acid) substituted variant thereof; of being of a certain size; and also being capable of specifically hybridizing to one of a particular group of nucleotide sequences.

Rules for the conservative amino acid substitution of artemin polypeptides are described on page 20, lines 11 - 26. Beginning from the artemin polypeptide sequences provided by SEQ ID NOS:3 - 5, and applying the substitution rules, a practitioner of ordinary skill could readily envision each and every one of the possible artemin polypeptides that would be encoded by the claimed polynucleotides. Although the number of possible sequences could be large, the skilled practitioner would be guided by the substitution rules provided in the specification as applied to only three polypeptide sequences.

However, to reduce the number of possible polynucleotides further, the claim has been amended to limit the nucleic acid molecule or fragment thereof to polynucleotides having at least 15, but no more than about 10,000 nucleotides.

Furthermore, a polynucleotide that lies within the scope of the claims must specifically hybridize to one of several mature human or mouse artemin polynucleotides, or their complements.

It is believed that such description of the claimed polynucleotides satisfies the written description requirement of §112, first paragraph, because there is no uncertainty as to which polynucleotides lie within the boundaries of the claim, and it is clear that the applicants had possession of the full scope of the claimed invention.

The essential goal of the description of the invention is to clearly convey the information that an applicant has invented the subject matter which is claimed. *In re Barker*, 194 USPQ 470 (CCPA 1970). The key issue is whether the specification describes the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor was in possession of the claimed invention. *Vas-Cath, Inc. v. Mahurkar*, 19 USPQ2d 1111 (Fed. Cir. 1991).

The Examiner's attention is drawn to the *Revised Interim Written Description Guidelines Training Material*, prepared for implementation of the *Interim Written Description Guidelines*, 114 Fed. Reg. 31639 - 32645 (June 15, 1998), where, in Example 9 (Hybridization), it is shown that the written description requirement is satisfied when a claim drawn to an isolated nucleic acid describes the nucleotide as hybridizing to a specific sequence under highly stringent hybridization conditions. In the same manner, present claims 12, 15, 16, 19 - 23 and 25 - 27 now describe the polynucleotides that encode artemin as specifically hybridizing to one of several specific sequences.

Therefore, it is maintained that a skilled practitioner would be able to determine with precision the scope of the nucleic acids that are described in the claims. Accordingly, it is respectfully requested that the rejection of claims 12, 15, 16, 19 - 23 and 25 - 27 be reconsidered and withdrawn.

Rejection of claim 21 under 35 USC §112, first paragraph, as lacking written description.

It is respectfully requested that the rejection of claim 21 under 35 USC §112, first paragraph, as lacking written description be reconsidered in view of the amendment to claim 21 and upon consideration of the reasons discussed below and be withdrawn.

The claim has been amended to describe the ATCC deposit in terms of the ATCC designation number for the plasmid deposited on December 22, 1998. A copy of the ATCC International Form indicating such deposit of plasmid phART is enclosed herewith.

Rejection of claims 12 and 15 - 27 under 35 USC §112, first paragraph, as lacking enablement for making and using the invention to the full scope of the claims.

It is respectfully requested that the rejection of claims 12 and 15 - 27 under 35 USC §112, first paragraph, as lacking enablement for making and using the invention to the full scope of the claims be reconsidered in view of the amendment of the claims and upon consideration of the reasons discussed below and be withdrawn.

In the Action, it is argued that claims 12 and 15 - 27 were not enabled for the full scope of all pan-growth factors, or for nucleic acids encoding "fragments" of artemin polypeptides.

Claim 12 is the only claim that describes pan-growth factors. The claim has now been amended to describe the polynucleotide encoding the artemin segment of a claimed pan-growth factor as being limited in size (from encoding as few as 8 amino acids, up to 10,000 nucleotides), and being capable of specifically hybridizing with one of several specified sequences. In addition, the claim has been amended to specify that it is the active domain of the non-artemin TGF- β that is to be encoded. It is believed that the identity of the active domain of non-artemin TGF- β growth factors were well known in the art and would have been easily determined by a skilled practitioner from the literature that was available at the time of the invention. In fact, in the specification at Figure 4 and at page 31, line 20 to page 32, line 18, the construction and characteristics of such pan-growth factors are described in detail.

Claims 12, 15 and 17 have been found to lack enablement because they include nucleic acid sequences that encode "fragments" of artemin polypeptides. It is argued that no functional properties or structural domains have been taught to provide guidance for the selection of such fragments, and, therefore, a skilled practitioner would be unable to successfully make and use such fragments.

The meaning of a "fragment" of an artemin polypeptide is described in detail in the specification at page 21, line 16 to page 22, line 9. Each of claims 12, 15 and 17 have been amended to describe the nucleic acid sequences that encode such fragments of artemin as encoding a fragment of a certain size and having the functional property of specifically hybridizing to a specific nucleotide sequence. Therefore, as discussed above, the skilled practitioner would be guided to nucleotide sequences for such "fragments" that were derived from a nucleotide sequence encoding an artemin polypeptide; that such sequences were of a certain size; and that such sequences must specifically hybridize to a certain specified sequence. In light of the amendments to the claims, it is believed that a skilled practitioner would be able to successfully make and use nucleotides encoding such fragments.

Accordingly, it is respectfully requested that this rejection be reconsidered and withdrawn.

Rejection of claims 15 - 24 and 26 under 35 USC §112, first paragraph, as lacking enablement for making and using the invention to the full scope of the claims.

It is respectfully requested that the rejection of claims 15 - 24 and 26 under 35 USC §112, first paragraph, as lacking enablement for making and using the invention to the full scope of the claims be reconsidered in view of the amendment of the claims and upon consideration of the reasons discussed below and be withdrawn.

The claims are rejected on the grounds that the specification does not teach how an artemin polypeptide could be encoded by the complement of nucleic acid sequences that encode artemin.

The language of the affected claims have been amended to clarify that it is only the nucleotide sequence that encodes artemin that is capable of that function, and not the complement of that sequence. It is believed that this amendment obviates the grounds for this rejection, and it is respectfully requested that the rejection be reconsidered and withdrawn.

Rejection of claims 12, 16 - 18, 23, 25 and 26 under 35 USC §112, second paragraph, as being indefinite.

It is respectfully requested that the rejection of claims 12, 16 - 18, 23, 25 and 26 under 35 USC §112, second paragraph, as being indefinite be reconsidered in view of the amendment of the claims and upon consideration of the reasons discussed below and be withdrawn.

Claim 12 was rejected as being unclear because it could not be determined if the fragment of at least 8 contiguous amino acids referred to the artemin sequence or to the pan-growth factor. Claim 12 has been amended to clarify that the fragment of at least 8 contiguous amino acids refers to the artemin sequence. Similarly, claim 25 has been amended to clarify that the fragment belongs to the artemin polypeptide sequence.

Claim 23 has been amended to replace the recitation of SEQ ID NO:41 with SEQ ID NO:40, and to replace SEQ ID NO:42 with SEQ ID NO:41. In the Action, it was correctly noted that SEQ ID NO:42 was not an amino acid sequence. The amendment corrects typographical errors in the claim.

Claim 16 has been amended to clarify that it is the artemin protein that is "mature", rather than the nucleotide sequence by which it is encoded. The claim has also been amended to clarify that it is only the nucleotide sequence that encodes artemin, rather both the sequence and the complement of such sequence. The Action also objected to the term "hybridizes" as being indefinite. However, the terms that are used in the claim are "specifically hybridizes", and the meaning of these terms, as they are used in this application, are defined in the specification, at page 29, line 26 - page 30, line 13. It is believed that this definition agrees with the meaning that these terms are generally understood to have in the art. Accordingly, it is maintained that a skilled practitioner, upon reading the specification and claims, would readily understand the meaning of the terms "specifically hybridizes". Accordingly, it is respectfully requested that this rejection be reconsidered and withdrawn.

For the reasons given above for claim 16, it is requested that the rejection of claims 17 and 18 also be withdrawn.

The Action has objected to claim 26 on several grounds. Claim 26 has been amended as suggested in the Action to read as an independent claim.

Rejection of claims 12, 15 and 16 under 35 USC §102(a) as being anticipated by GenBank disclosure AC005038, Waterston (1998).

It is respectfully requested that the rejection of claims 12, 15 and 16 under 35 USC §102(a) as being anticipated by GenBank disclosure AC005038, Waterston (1998), be reconsidered in view of the amendments to the claims and upon consideration of the reasons discussed below and be withdrawn.

Claims 12, 15 and 16 have been amended to describe the polynucleotide as containing no more than about 10,000 nucleotides, whereas the nucleic acid that is disclosed in AC005038 includes 191,332 nucleotides. Accordingly, it is maintained that the claims as amended do not read on the nucleic acid of AC005038, and it is respectfully requested that the rejection be reconsidered and withdrawn.

Rejection of claims 19 and 20 under 35 USC §103(a) as being obvious in view of GenBank disclosure AC005038, Waterston (1998).

It is respectfully requested that the rejection of claims 19 and 20 under 35 USC §103(a) as being obvious in view of GenBank disclosure AC005038, Waterston (1998), be reconsidered in view of the amendments to the claims and upon consideration of the reasons discussed below and be withdrawn.

Claims 19 and 20 both incorporate the limitations of claim 15, which provide that the claimed polynucleotide contains not over about 10,000 nucleotides. Since the AC005038 disclosure does not teach the polynucleotide of claim 15, as discussed above, it would not be obvious to arrive at the vector of claim 19, or the host cell of claim 20, both of which require the presence of the nucleic acid of claim 15. Accordingly, it is respectfully requested that this rejection be reconsidered and withdrawn.

Draftsperson's Patent Drawing Review:

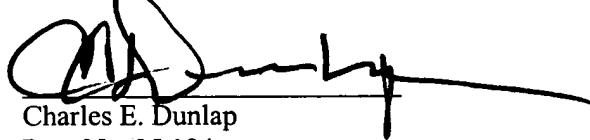
The Notice of Draftsperson's Patent Drawing Review on PTO form 948 is respectfully acknowledged. The Applicant intends to correct the drawings as required by the Draftsperson, but it is requested that this requirement be held in abeyance until such time as the substantive grounds for rejection have been resolved and allowable subject matter has been defined.

Request for reconsideration:

It is respectfully requested that the accompanying Information Disclosure Statement and the amendments described above be entered into the case and that the claims be reconsidered in view of the amendments and the remarks that follow the amendments. It is believed that the claims are now in

condition for allowance and such action is hereby respectfully requested. If it is deemed that some or all of the claims are not in condition for allowance, it is specifically requested that the Examiner contact the undersigned by telephone at the number given below in order that any remaining issues may be resolved.

Respectfully submitted,



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August 16, 2000